

What is claimed is:

1. A pharmaceutical composition comprising N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or a pharmaceutically acceptable salt thereof in combination with one or more pharmaceutically acceptable carriers, wherein at least some of N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof is in granulated form.

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10 2. A composition as claimed in claim 1 wherein substantially all of N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof is in granulated form.

15 3. A composition as claimed in claim 1 wherein 50% or more by weight or by volume of the granules including N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof have a particle size of ≥ 100 microns (micrometres) .

20 4. A composition as claimed in claim 1 wherein 50% or more by weight or by volume of the granules including N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof have a particle size of ≥ 250 microns .

25 5. A composition as claimed in claim 1 wherein 50% or more by weight or by volume of the granules including N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof have a particle size of 100 to 1000 microns.

30 6. A composition as claimed in claim 1 or 3 wherein 90% or more by weight or by volume of the granules including N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof have a particle size of ≥ 10 microns (micrometres).

35 7. A composition as claimed in claim 1 or 4 wherein 90% or more by weight or by volume of the granules including N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof have a particle size of ≥ 50 microns (micrometres).

40 8. A composition as claimed in claim 1 wherein 50% or more by weight or by volume of the particles of N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-

[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof have a particle size of \leq 50 microns (micrometres).

9. A composition as claimed in claim 1 wherein 10% or more by weight or by

5 volume of the particles of N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof have a particle size of \leq 10 microns (micrometres).

10. A composition as claimed in claim 1 wherein 50% or more by weight or by

10 volume of the granules including N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof have a particle size of \geq 100 microns (micrometres); and wherein 10% or more by weight or by volume of the particles of N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof have a particle size of \leq 10 microns.

15 11. A composition as claimed in claim 1 or 3 wherein N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof is present in the composition in at least 3.5 weight % by weight of the

20 composition.

25 12. A composition as claimed in claim 1 or 3 wherein N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof is present in the composition in at least 4 weight % by weight of the

composition.

30 13. A composition as claimed in claim 1 or 3 wherein N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof comprises the hydrochloride salt of N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide.

14. A composition as claimed in claim 1 or 3 wherein the granules containing

N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof also contain a filler (diluent).

35 15. A composition as claimed in claim 14 wherein the filler (diluent) is abrasive.

16. A composition as claimed in claim 14 wherein the filler (diluent) is

insoluble, practically insoluble, very slightly soluble or slightly soluble in water and/or ethanol.

17. A composition as claimed in claim 14 wherein the filler (diluent) is insoluble or practically insoluble in water and/or ethanol.

18. A composition as claimed in claim 14 wherein the filler comprises any pharmaceutically acceptable metal (e.g. calcium or magnesium) salt which is insoluble, practically insoluble, very slightly soluble or slightly soluble in water and/or ethanol.

19. A composition as claimed in claim 1 or 3 wherein the granules containing N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof also contain a filler (diluent) comprising CaHPO_4 and/or $\text{Ca}_3(\text{PO}_4)_2$.

20. A composition as claimed in claim 16 or 19, wherein the weight ratio of filler to drug in the composition or granules is at least 1:3.

21. A composition as claimed in claim 16, wherein the filler is present in from 15 to 85% by weight of the composition.

22. A composition as claimed in claim 1 or 3 including a binder.

23. A composition as claimed in claim 22 wherein the binder comprises hydroxypropylmethylcellulose.

24. A composition as claimed in claim 1, 3 or 19 including an excipient which acts as a compression and/or granulation aid.

25. A composition as claimed in claim 1, 3 or 19 being a tablet, or a capsule containing said composition.

26. A process of making a pharmaceutical composition comprising N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or a pharmaceutically acceptable salt thereof in combination with one or more pharmaceutically acceptable carriers, the method comprising forming at least some of N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof into granules.

27. A method as claimed in claim 26 comprising mixing some or all of N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-

carboxamide or salt thereof with a filler (diluent), and optionally a binder and/or a compression and/or granulation aid, before granulation.

28. A method as claimed in claim 27 wherein the granules are formed in the
5 presence of a granulating solvent (i.e. using a "wet granulation" process).

29. A method as claimed in claim 28 wherein the filler is insoluble, practically insoluble, very slightly soluble or slightly soluble in the granulation solvent.

10 30. A method as claimed in claim 29 wherein after formation the granules are milled to a particle size suitable for use in tablets or capsules.

15 31. A method as claimed in claim 26 or 30 wherein, after being formed and optionally milled, the granules are mixed with other pharmaceutically acceptable excipient(s) and compressed into tablets or filled into capsules.

20 32. A method of making a pharmaceutical composition comprising N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or a pharmaceutically acceptable salt thereof in combination with one or more pharmaceutically acceptable carriers,

the method comprising:

(a) dissolving N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof in ethanol or an ethanol-containing solvent to form a solution,

25 (b) crystallising N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof from the solution by addition of a C₅-C₁₀ hydrocarbon and/or a solvent containing a C₅-C₁₀ hydrocarbon, and

30 (c) forming at least some of N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof into granules.

33. A method as claimed in claim 32 wherein N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof comprises the hydrochloride salt of N-[(1-nbutyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide.

34. A method as claimed in claim 33 comprising the additional step after formation of the granules of (d) mixing the granules with other pharmaceutically acceptable excipient(s) and compressed into tablets or filled into capsules.